10/626,173

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     (FILE 'HOME' ENTERED AT 09:54:24 ON 14 SEP 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:54:57 ON 14 SEP 2004
L1            14 S "CARK"
L2             4 S "CARDIAC-RELATED ANKYRIN-REPEAT"
L3            14 S L1 OR L2
L4       3904375 S MODULATOR? OR INHIBITOR? OR ACTIVATOR?
L5       8679450 S IDENTIF? OR FIND? OR SCREEN?
L6        638317 S L4 AND L5
L7             0 S L3 AND L6
L8            13 DUP REM L3 (1 DUPLICATE REMOVED)
L9             2 S HUMAN AND L8
                 E RAJU J/AU
L10          109 S E3
L11            2 S L3 AND L10
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TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	May 12	EXTEND option available in structure searching
NEWS 4	May 12	Polymer links for the POLYLINK command completed in REGISTRY
NEWS 5	May 27	New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
NEWS 6	May 27	CAplus super roles and document types searchable in REGISTRY
NEWS 7	Jun 28	Additional enzyme-catalyzed reactions added to CASREACT
NEWS 8	Jun 28	ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG, and WATER from CSA now available on STN(R)
NEWS 9	Jul 12	BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS
NEWS 10	Jul 30	BEILSTEIN on STN workshop to be held August 24 in conjunction with the 228th ACS National Meeting
NEWS 11	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS 12	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 13	AUG 02	STN User Update to be held August 22 in conjunction with the 228th ACS National Meeting
NEWS 14	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 15	AUG 04	Pricing for the Save Answers for SciFinder Wizard within STN Express with Discover! will change September 1, 2004
NEWS 16	AUG 27	BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 17	AUG 27	BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
NEWS 18	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS 19	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS 20	SEP 01	New display format, HITSTR, available in WPIDS/WPINDEX/WPIX

NEWS EXPRESS	JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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result in loss of user privileges and other penalties.

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FILE 'HOME' ENTERED AT 09:54:24 ON 14 SEP 2004

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 09:54:57 ON 14 SEP 2004

FILE 'EMBASE' ENTERED AT 09:54:57 ON 14 SEP 2004

FILE 'BIOSIS' ENTERED AT 09:54:57 ON 14 SEP 2004

FILE 'BIOTECHDS' ENTERED AT 09:54:57 ON 14 SEP 2004

FILE 'SCISEARCH' ENTERED AT 09:54:57 ON 14 SEP 2004

FILE 'HCAPLUS' ENTERED AT 09:54:57 ON 14 SEP 2004

FILE 'NTIS' ENTERED AT 09:54:57 ON 14 SEP 2004

FILE 'LIFESCI' ENTERED AT 09:54:57 ON 14 SEP 2004

=> s "CARK"
L1 14 "CARK"

=> s "cardiac-related ankyrin-repaet"
<------User Break------>

SEARCH ENDED BY USER

=> s "cardiac-related ankyrin-repeat"
L2 4 "CARDIAC-RELATED ANKYRIN-REPEAT"

=> s l1 or l2
L3 14 L1 OR L2

=> s modulator? or inhibitor? or activator?
L4 3904375 MODULATOR? OR INHIBITOR? OR ACTIVATOR?

=> s identif? or find? or screen?
L5 8679450 IDENTIF? OR FIND? OR SCREEN?

=> s l4 and l5
L6 638317 L4 AND L5

=> s l3 and l6
L7 0 L3 AND L6

=> dup rem l3
PROCESSING COMPLETED FOR L3
L8 13 DUP REM L3 (1 DUPLICATE REMOVED)

=> d 1-13 ibib ab

L8 ANSWER 1 OF 13 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:74544 BIOSIS
DOCUMENT NUMBER: PREV200400077782
TITLE: **CARK** protein and nucleic acid molecules and uses therefor.
AUTHOR(S): Raju, Jeyaseelan [Inventor, Reprint Author]
CORPORATE SOURCE: ASSIGNEE: Millennnium Pharmaceuticals, Inc., Cambridge, MA, USA
PATENT INFORMATION: US 6660490 December 09, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec 9 2003) Vol. 1277, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Feb 2004
Last Updated on STN: 4 Feb 2004
AB The invention provides isolated nucleic acids molecules, designated **CARK** nucleic acid molecules. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing **CARK** nucleic acid molecules, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a **CARK** gene has been introduced or disrupted. The invention still further provides isolated **CARK** proteins, fusion proteins, antigenic peptides and anti-**CARK** antibodies. Diagnostic methods utilizing compositions of the invention are also provided.

L8 ANSWER 2 OF 13 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-13047 BIOTECHDS
TITLE: Novel isolated **cardiac-related ankyrin-repeat** protein kinase polypeptide, useful for treating cellular growth related disorders which include cardiovascular disorders and proliferative and/or differentiative disorders;
vector-mediated gene transfer and expression in host cell for recombinant protein production for use in disease diagnosis, gene therapy and pharmacogenomics
AUTHOR: RAJU J
PATENT ASSIGNEE: MILLENNIUM PHARM INC
PATENT INFO: WO 2003020912 13 Mar 2003
APPLICATION INFO: WO 2002-US28300 4 Sep 2002
PRIORITY INFO: US 2001-947199 5 Sep 2001; US 2001-947199 5 Sep 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-290188 [28]
AB DERWENT ABSTRACT:
NOVELTY - An isolated **cardiac-related ankyrin -repeat** protein kinase (**CARK**) polypeptide (I), comprising an allelic variant of a polypeptide having a sequence (S1) of 835 amino acids (aa), encoded by a nucleic acid molecule (NA) that hybridizes to a sequence (S2) of 3025, 2505 or 3026 base pairs, or a polypeptide encoded by a NA 60% homologous to S2, or fragment of S1, where S1 and S2 are given in specification, is new.
DETAILED DESCRIPTION - (I) is selected from a naturally occurring allelic variant of S1 encoded by a NA which hybridizes to NA comprising

S2 under stringent conditions, a polypeptide encoded by a NA comprising a sequence which is at least 60% homologous to S2, a fragment comprising at least 15 contiguous (aa)s of S1, and a polypeptide comprising an (aa) sequence which is at least 60% homologous to S1. INDEPENDENT CLAIMS are also included for the following: (1) isolated NA (II) selected from a NA comprising a sequence of S2, a NA which encodes a polypeptide comprising S1, a NA comprising the sequence contained in the plasmid deposited with ATCC as Accession Number PTA-1530, a NA which encodes the naturally occurring allelic variant of S1, a NA comprising a sequence which is at least 60% homologous to S2 or its complement, a NA comprising a fragment of at least 467 nucleotides of S2 or its complement, a NA which encodes a polypeptide comprising a sequence at least about 60% homologous to S1, and a NA which encodes a fragment of S1, where the fragment comprises at least 15 contiguous (aa)s of S1; (2) an isolated NA which hybridizes to (II) under stringent conditions; (3) isolated NA comprising a sequence which is complementary to the sequence of (II); (4) isolated NA comprising (II), and a nucleotide sequence encoding a heterologous polypeptide; (5) vector (III) comprising (II); (6) host cell (HC) transfected with (III); (7) antibody (IV) which selectively binds (I); (8) production of (I); (9) detecting (M1) the presence of (II) in a sample by contacting the sample with a nucleic acid probe or primer which selectively hybridizes to (II), and determining whether the probe or primer binds to (II) in the sample; (10) kit (V) comprising a compound which selectively binds to (I) or hybridizes to (II), and instructions for use; and (11) modulating (M2) the activity of (I) by contacting (I) or a cell expressing (I) with a compound which binds to (I).

WIDER DISCLOSURE - Also disclosed are: (1) isolated NA antisense to (II); (2) diagnostic assay for identifying the presence or absence of a genetic alteration characterized by at least one of aberrant modification or mutation of a gene encoding a **CARK** protein, mis-regulation of the gene, and aberrant post-translational modification of a **CARK** protein; (3) nucleic acid molecule that differs from S2, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-1530; (4) a non-human ortholog of (I); (5) nucleic acid molecule encoding (I) that contains changes in (aa) residues that are not essential for activity; (6) **CARK** chimeric or fusion proteins; and (7) agent which modulates expression or activity of (I).

BIOTECHNOLOGY - Preparation: (I) is produced by culturing HC in an appropriate culture medium to produce (I) (claimed). Preferred Polypeptide: (I) further comprises heterologous (aa) sequences. Preferred Vector: (III) is an expression vector. Preferred Method: In M1, the sample comprises mRNA molecules and is contacted with a nucleic acid probe.

ACTIVITY - Cardiant; Hypotensive; Cytostatic. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - (IV) is useful for detecting the presence of (I) in a sample by contacting the sample with (IV), and determining whether (IV) binds to (I) in the sample. (I) is useful for identifying a compound which binds to (I) by contacting (I), or a cell expressing (I) with a test compound, and determining whether (I) binds to the test compound. (I) is useful for identifying a compound which modulates the activity of (I) by contacting (I) with a test compound and determining the effect of the test compound on the activity of (I) (claimed). (I) or (II) is useful as modulating agents for regulating a variety of cellular processes, e.g., cardiac cellular process, for modulating the phosphorylation state of a **CARK** molecule or one or more proteins involved in cellular growth or differentiation, for modulating cell behavior or as targets and therapeutic agents controlling cardiac cell proliferation, differentiation, hypertrophy and migration, for modulating intra-or inter-cellular signaling and/or gene transcription, for modulating cell proliferation, growth, differentiation, survival and/or migration, for regulating transmission of signals from cellular receptors, for

modulating entry of cells, e.g., cardiac precursor cells, into mitosis, or for regulating cytoskeletal function. (I) or (II) is useful for treating cellular growth related disorders which include cardiovascular disorders (such as heart failure, hypertension), and proliferative and/or differentiative disorders (such as cancer). (I), (II) or (IV) is useful in screening assays, detection assays (e.g., chromosomal mapping, tissue typing, forensic biology), predictive medicine (e.g., diagnostic assays, prognostic assays, monitoring clinical trials and pharmacogenomics), and in methods of treatment (e.g., therapeutic and prophylactic). (I) is useful as an immunogen to generate antibodies that bind (I). (I) is useful to screen for naturally occurring **CARK** substrates, and to screen for drugs or compounds which modulate **CARK** activity. (I) is useful as a bait protein in a yeast two-hybrid or three-hybrid assay and to identify other proteins which bind to or interact with **CARK** and or involved in the **CARK** activity. (II) is useful as hybridization probe to identify (II), or as polymerase chain reaction (PCR) primer for the amplification or mutation of (II). (II) is useful in gene therapy, to express (I), to detect **CARK** mRNA or a genetic alteration in a **CARK** gene, and to modulate **CARK** activity. (II) is useful to map their respective genes on a chromosome, e.g. to locate gene regions associated with genetic disease or to associate **CARK** with the disease, to identify an individual from a minute biological sample (tissue typing), and to aid in forensic identification of the biological sample. (I) or (II) is useful as a query sequence to perform a search against public databases to, for example, identify other family members or related sequences. HC is useful for producing non-human transgenic animals. (IV) is useful to isolate and purify (I), to detect (I) and to diagnostically monitor protein levels in tissue as part of a clinical testing procedure.

ADMINISTRATION - A pharmaceutical composition comprising (I), (II) or (V) is administered by parenteral, e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (topical), transmucosal, or rectal route at a dose of 0.001-30 mg/kg, preferably 1-10 mg/kg, more preferably 5-6 mg/kg.

EXAMPLE - Identification and characterization of the genes encoding human **cardiac-related ankyrin-repeat** protein kinase (**CARK**) and rat **CARK** was as follows: The human **CARK** gene was isolated from cDNA library which was prepared from tissue obtained from subjects suffering from congestive heart failure of ischemic and idiopathic origin. Briefly, a cardiac tissue sample was obtained from a biopsy of four patients suffering from congestive heart failure. mRNA was isolated from the cardiac tissue and a cDNA library was prepared. Positive clones were isolated from these libraries using appropriate primers. The sequence of the positive clone was determined and found to contain an open reading frame. The nucleotide sequence encoding the human **CARK** protein comprised about 3025 nucleic acids. The protein encoded by this nucleic acid comprised abut 835 (aa)s. A clone containing the rat **CARK** cDNA was also identified. The nucleotide sequence encoding the rat **CARK** protein comprised about 3026 nucleic acids. The protein encoded by this nucleic acid comprised about 835 (aa)s. (158 pages)

L8 ANSWER 3 OF 13 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:85983 BIOSIS
DOCUMENT NUMBER: PREV200300085983
TITLE: **CARK** protein and nucleic acid molecules and uses therefor.
AUTHOR(S): Raju, Jeyaseelan [Inventor, Reprint Author]
CORPORATE SOURCE: ASSIGNEE: Millennium Pharmaceuticals, Inc.
PATENT INFORMATION: US 6500654 December 31, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec 31 2002) Vol. 1265, No. 5. http://www.uspto.gov/web/menu/patdata.html. e-file.

ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Feb 2003
Last Updated on STN: 6 Feb 2003

AB The invention provides isolated nucleic acids molecules, designated **CARK** nucleic acid molecules. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing **CARK** nucleic acid molecules, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a **CARK** gene has been introduced or disrupted. The invention still further provides isolated **CARK** proteins, fusion proteins, antigenic peptides and anti-**CARK** antibodies. Diagnostic methods utilizing compositions of the invention are also provided.

L8 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:696560 HCAPLUS
DOCUMENT NUMBER: 137:227755
TITLE: Protein and cDNA sequences of novel human and rat **CARK** (**cardiac-related ankyrin repeat** protein kinase) and uses thereof
INVENTOR(S): Raju, Jeyaseelan
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 94 pp., Cont.-in-part of U.S. Ser. No. 458,457.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002127684	A1	20020912	US 2001-947199	20010905
US 6660490	B2	20031209		
US 6261818	B1	20010717	US 1999-291839	19990414
US 6500654	B1	20021231	US 1999-458457	19991210
WO 2003020912	A2	20030313	WO 2002-US28300	20020904
WO 2003020912	A3	20030828		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1430070	A2	20040623	EP 2002-757606	20020904
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004110232	A1	20040610	US 2003-626173	20030724

PRIORITY APPLN. INFO.:

US 1998-111938P	P	19981211
US 1999-291839	A2	19990414
US 1999-458457	A2	19991210
US 2001-947199	A	20010905
WO 2002-US28300	W	20020904

AB The invention provides human and rat protein and cDNA sequences encoding **CARK** (**cardiac-related ankyrin repeat** protein kinase). The invention also provides antisense

nucleic acid mols., recombinant expression vectors containing **CARK** nucleic acid mols., host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a **CARK** gene has been introduced or disrupted. The invention still further provides isolated **CARK** proteins, fusion proteins, antigenic peptides and anti-**CARK** antibodies. Diagnostic methods utilizing compns. of the invention are also provided.

L8 ANSWER 5 OF 13 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2002:341659 SCISEARCH
THE GENUINE ARTICLE: 540HT
TITLE: Anemia prevention and control in four central Asian republics and Kazakhstan
AUTHOR: Gleason G R (Reprint); Sharmanov T
CORPORATE SOURCE: IDPAS, Iron Deficiency Project Advisory Serv, 126 Curtis St, Medford, MA 02155 USA (Reprint); IDPAS, Iron Deficiency Project Advisory Serv, Medford, MA 02155 USA; Nutr Inst Kazakhstan, Almaty 480008, Kazakhstan
COUNTRY OF AUTHOR: USA; Kazakhstan
SOURCE: JOURNAL OF NUTRITION, (APR 2002) Vol. 132, No. 4, Supp. [S], pp. 867S-870S.
Publisher: AMER INST NUTRITION, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0022-3166.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 0

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Kazakhstan and the central Asian republics of Uzbekistan, the Kyrgyz Republic, Tajikistan and Turkmenistan have developed anemia prevention and control (APC) policies based on multiple interventions, including education and promotion, oral supplementation of high risk groups and fortification of wheat flour with iron and other micronutrients. These national strategies are aimed at reducing the prevalence of anemia and iron deficiency among young children and women of child-bearing age. Strategy development has been assisted by funding and technical assistance from the United Nations Children's Fund (UNICEF) with additional technical support from the International Nutrition Foundation, the United Nations University and various national institutions. These countries have been among the most advanced in adopting national strategies that include multiple interventions in an overall package, and national interest in APC remains high. However, reviews of APC activities conducted in 2001 suggests the need for modification and enhancement of current efforts and for a shift to national-level actions if these countries are to progress toward current and future goals. Increased commitment and determination, by both national groups and international organizations, are required to achieve and sustain improvement in micronutrient nutrition.

L8 ANSWER 6 OF 13 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:420615 BIOSIS
DOCUMENT NUMBER: PREV200100420615
TITLE: **CARK** protein and nucleic acid molecules and uses therefor.
AUTHOR(S): Raju, Jeyaseelan [Inventor, Reprint author]
CORPORATE SOURCE: Acton, MA, USA
ASSIGNEE: Millennium Pharmaceuticals, Inc.
PATENT INFORMATION: US 6261818 July 17, 2001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (July 17, 2001) Vol. 1248, No. 3. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

ENTRY DATE: Entered STN: 5 Sep 2001
Last Updated on STN: 22 Feb 2002

AB The invention provides isolated nucleic acids molecules, designated **CARK** nucleic acid molecules. The invention also provides antisense nucleic acid molecules, recombinant expression vectors containing **CARK** nucleic acid molecules, host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a **CARK** gene has been introduced or disrupted. The invention still further provides isolated **CARK** proteins, fusion proteins, antigenic peptides and anti-**CARK** antibodies. Diagnostic methods utilizing compositions of the invention are also provided.

L8 ANSWER 7 OF 13 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
DUPLICATE 1
ACCESSION NUMBER: 2000-11607 BIOTECHDS
TITLE: New polynucleotide encoding **cardiac-related ankyrin-repeat** protein-kinase, useful for treating disorders such as cardiovascular disorders, e.g. heart failure and cell differentiation disorders, e.g. cancer ;
vector-mediated gene transfer and expression in host cell, antibody, DNA probe and DNA primer
AUTHOR: Raju J
PATENT ASSIGNEE: Millennium-Pharm.
LOCATION: Cambridge, MA, USA.
PATENT INFO: WO 2000034330 15 Jun 2000
APPLICATION INFO: WO 1999-US29465 10 Dec 1999
PRIORITY INFO: US 1999-291839 14 Apr 1999; US 1998-111938 11 Dec 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-431275 [37]
AB A polynucleotide encoding a **cardiac-related ankyrin-repeat** protein-kinase (EC-2.7.1.37) (**CARK**) containing a sequence of 3,025, 2,505, 3,026 or 2,505 bp as defined in the specification, is new. Also claimed are: a nucleic encoding a protein of 835 amino acids; an expression vector; a host cell; a method of producing the protein; an antibody; a method for detecting the presence of the protein; a method for detecting the presence of the polynucleotide using a DNA probe or DNA primer; a kit containing a compound that specifically binds to the protein or polynucleotide; a method for identifying a compound that specifically binds to the protein; a method for modulating the activity of the protein; and a method for identifying a compound which modulates that activity of the protein. The polynucleotides is useful for detecting nucleic acid molecule especially mRNA in a sample, **CARK** encoded by the polynucleotide is useful for treating disorders associated with upregulation or downregulation of cellular proliferation such as disorders concerned with cardiovascular disorders and disorders associated with differentiation of cells such as cancer and sarcoma. (161pp)

L8 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:200376 HCAPLUS
DOCUMENT NUMBER: 126:197250
TITLE: Regulation of the O2-evolving mechanism during N2-fixation in the diazotrophic cyanobacterium Cyanothece sp. ATCC 51142
AUTHOR(S): Meunier, Pascal C.; Watters, James W.; Colon-Lopez, Milagros S.; Sherman, L. A.
CORPORATE SOURCE: Department of Biological Sciences, Purdue University, West Lafayette, IN, 47907, USA
SOURCE: Photosynthesis: From Light to Biosphere, Proceedings of the International Photosynthesis Congress, 10th, Montpellier, Fr., Aug. 20-25, 1995 (1995), Volume 2,

389-392. Editor(s): Mathis, Paul. Kluwer: Dordrecht, Neth.
CODEN: 64DFAW
DOCUMENT TYPE: Conference
LANGUAGE: English
AB N2 fixation by C. ATCC 51142 is controlled by a circadian rhythm. The capacity and the properties of O2 production by the S-state mechanism in cultures subjected to 12-h light/**cark** cycles were investigated. The peak of O2 evolution was found to be 12 h out of phase with N2 fixation. These results suggested that the stability of Mn centers in the dark, their sensitivity to the redox state of quinones, the capacity for O2 production, the photoreactivation capacity, and the presence of super-reduced S-states are all modulated in Cyanothece.

L8 ANSWER 9 OF 13 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 92:3159 SCISEARCH
THE GENUINE ARTICLE: GT369
TITLE: THE THEORY OF CYCLOTRON AUTORESONANCE KLYSTRON
AUTHOR: SMIRNOV G T (Reprint)
CORPORATE SOURCE: ACAD SCI USSR, URAL SCI CTR, INST ELECTROPHYS, SVERDLOVSK, USSR (Reprint)
COUNTRY OF AUTHOR: USSR
SOURCE: IZVESTIYA VYSSHIKH UCHEBNYKH ZAVEDENII RADIOFIZIKA, (1991) Vol. 34, No. 2, pp. 177.
ISSN: 0021-3462.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: ENGI
LANGUAGE: Russian
REFERENCE COUNT: 10
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A cyclotron autoresonance klystron (**CARK**), a new type of cyclotron autoresonance maser, is theoretically investigated. The formulae of efficiency, threshold current and optimum current are obtained with taken intoaccount and initial electron beam energy spread and pitch angle spread. It is shown, that the efficiency of the **CARK**, which is constructed bu the analogy with a two-resonator klystron, may be more than 50%, und the efficiency of the **CARK**, which is consructed bu the analogy with a three-resonator klystron, reaches 60%. The **CARK** realatively intensive to the electron beam quality. For example, in the powerful **CARK** the initial electron beam energy spread and pitch angle spread may amount several per cent without the sufficient loss of efficiency.

L8 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:562636 HCAPLUS
DOCUMENT NUMBER: 109:162636
TITLE: A catechol electrode based on spinach leaves
AUTHOR(S): Uchiyama, Shunichi; Tamata, Minoru; Tofuku, Yoshinobu; Suzuki, Shuichi
CORPORATE SOURCE: Dep. Environ. Eng., Saitama Inst. Technol., Saitama, 369-02, Japan
SOURCE: Analytica Chimica Acta (1988), 208(1-2), 287-90
CODEN: ACACAM; ISSN: 0003-2670
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Minced spinach leaf (Spinacea oleracea) has a high activity of catechol oxidase (dimerizing) (EC 1.1.3.14), which is utilized for the determination of catechol by coupling the spinach tissue with a Clark oxygen electrode. The calibration graph for catechol is linear over the range 2 + 10-5-8 + 10-4M (relative standard deviation 3%). The sensor retains its enzyme activity for at least 18 days. 4-Methylcatechol and glycolate interfere; glucose and ascorbate do not.

L8 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:429158 HCAPLUS
DOCUMENT NUMBER: 103:29158
TITLE: Evaluation of thin film properties by the coulostatic method
AUTHOR(S): Fukunaga, Akihiko; Ueda, Shigetomo; Suzuki, Masayuki
CORPORATE SOURCE: Negishi Refinery Inspect Sect., Nippon Pet. Refinery Co. Ltd., Yokohama, 235, Japan
SOURCE: Kinzoku Hyomen Gijutsu (1985), 36(5), 191-7
CODEN: KZHGAY; ISSN: 0026-0614
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The differential double layer capacitance and polarization resistance of the vapor-deposited thin films of Al and Al-Cu under various conditions were measured in **Cark** Lubs buffer solution (pH 7.2) by the coulostatic method, and compared with other films and bulk metals. The differential capacitance and polarization resistance represented the surface conditions of the films, therefore they are effective in evaluating the corrosion rate and estimating the depth of oxide films.

L8 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 1983:244189 BIOSIS
DOCUMENT NUMBER: PREV198376001681; BA76:1681
TITLE: DISTRIBUTION OF LARVAL GIZZARD SHAD DOROSOMA-CEPEDIANUM IN LAKE CARL-BLACKWELL OKLAHOMA USA.
AUTHOR(S): DOWNEY P [Reprint author]; TOETZ D
CORPORATE SOURCE: BOX 747, OUACHITA BAPTIST UNIV, ARKADELPHIA, ARKANSAS 71923, USA
SOURCE: American Midland Naturalist, (1983) Vol. 109, No. 1, pp. 23-33.
CODEN: AMNAAF. ISSN: 0003-0031.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Year-class formation in fishes in poorly understood because of the difficulty of estimating abundance of fish larvae. The temporal and spatial distribution of gizzard shad larvae (D. cepedianum) in Lake **Cark** Blackwell (LCB), Oklahoma is described to provide a basis for future efforts at sampling larvae of this important forage fish in reservoirs. Larvae were sampled with a net (mouth 0.20 m2) towed in front of a boat at night at depths of 0 (surface), 3, 5 and 7 m between April and July 1977. Wind direction and velocity, cited by other workers as decisive in determining fish larval distribution, were related to patterns of larval abundance. Larvae were captured by the gear at a length of .apprx. 5 mm, but were not captured after they reached slightly more than 15 mm .apprx. 10 wk later. Larval density was highest, .apprx. 100 m-3, during late May and early June. Larvae were captured near the surface at the outset and were apparently passively distributed by winds. The rest of the time they were most abundant at 3 m, near the compensation point, suggesting maintenance of a preferred position in the water column. Estimates of larval shad density taken offshore were the same as estimates nearshore in areas of the lake with either very high or low densities. The dendritic configuration of the lake basin precluded prediction of horizontal or vertical patterns of distribution of shad larvae. Accurate estimates of density will be possible only by intensively sampling all areas of the lake throughout the season. Stratified random sampling programs for shad larvae are not now reasonable for dendritic lakes such as LCB.

L8 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1982:51293 HCAPLUS
DOCUMENT NUMBER: 96:51293
TITLE: Changes and significance in natural nitrogen-15

abundance in residual nitrogen fertilizer studies
AUTHOR(S): Karamanos, R. E.; Rennie, D. A.
CORPORATE SOURCE: Dep. Soil Sci., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.
SOURCE: Canadian Journal of Soil Science (1981), 61(4), 553-9
CODEN: CJSSAR; ISSN: 0008-4271
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The systematic decline in δa15N (per mill 15N excess) of plant material with application of fertilizer under field conditions was verified in a growth chamber experiment with wheat on Orthic Dark Brown Chernozemic soil columns. The δa15N of nitrate-N in the zones of the high nitrate-N accumulation was lower than that of the soil derived nitrate-N but not necessarily lower than the δa15N of fertilizer material as was the case in previously reported field expts. Calcn. of the fate of the fertilizer N based on the principle of isotopic dilution provided semiquant. ests. of the added N found in the plant, the soil, and the leachate.

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(FILE 'HOME' ENTERED AT 09:54:24 ON 14 SEP 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:54:57 ON 14 SEP 2004

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L1          14 S "CARK"
L2           4 S "CARDIAC-RELATED ANKYRIN-REPEAT"
L3          14 S L1 OR L2
L4     3904375 S MODULATOR? OR INHIBITOR? OR ACTIVATOR?
L5     8679450 S IDENTIF? OR FIND? OR SCREEN?
L6      638317 S L4 AND L5
L7           0 S L3 AND L6
L8          13 DUP REM L3 (1 DUPLICATE REMOVED)
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=> s human and l8

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L9           2 HUMAN AND L8
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=> d 1-2 ibib ab

L9 ANSWER 1 OF 2 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-13047 BIOTECHDS
TITLE: Novel isolated **cardiac-related ankyrin-repeat** protein kinase polypeptide, useful for treating cellular growth related disorders which include cardiovascular disorders and proliferative and/or differentiative disorders;
vector-mediated gene transfer and expression in host cell for recombinant protein production for use in disease diagnosis, gene therapy and pharmacogenomics
AUTHOR: RAJU J
PATENT ASSIGNEE: MILLENNIUM PHARM INC
PATENT INFO: WO 2003020912 13 Mar 2003
APPLICATION INFO: WO 2002-US28300 4 Sep 2002
PRIORITY INFO: US 2001-947199 5 Sep 2001; US 2001-947199 5 Sep 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-290188 [28]
AB DERWENT ABSTRACT:
NOVELTY - An isolated **cardiac-related ankyrin -repeat** protein kinase (**CARK**) polypeptide (I), comprising an allelic variant of a polypeptide having a sequence (S1) of 835 amino acids (aa), encoded by a nucleic acid molecule (NA) that hybridizes to a sequence (S2) of 3025, 2505 or 3026 base pairs, or a

polypeptide encoded by a NA 60% homologous to S2, or fragment of S1, where S1 and S2 are given in specification, is new.

DETAILED DESCRIPTION - (I) is selected from a naturally occurring allelic variant of S1 encoded by a NA which hybridizes to NA comprising S2 under stringent conditions, a polypeptide encoded by a NA comprising a sequence which is at least 60% homologous to S2, a fragment comprising at least 15 contiguous (aa)s of S1, and a polypeptide comprising an (aa) sequence which is at least 60% homologous to S1. INDEPENDENT CLAIMS are also included for the following: (1) isolated NA (II) selected from a NA comprising a sequence of S2, a NA which encodes a polypeptide comprising S1, a NA comprising the sequence contained in the plasmid deposited with ATCC as Accession Number PTA-1530, a NA which encodes the naturally occurring allelic variant of S1, a NA comprising a sequence which is at least 60% homologous to S2 or its complement, a NA comprising a fragment of at least 467 nucleotides of S2 or its complement, a NA which encodes a polypeptide comprising a sequence at least about 60% homologous to S1, and a NA which encodes a fragment of S1, where the fragment comprises at least 15 contiguous (aa)s of S1; (2) an isolated NA which hybridizes to (II) under stringent conditions; (3) isolated NA comprising a sequence which is complementary to the sequence of (II); (4) isolated NA comprising (II), and a nucleotide sequence encoding a heterologous polypeptide; (5) vector (III) comprising (II); (6) host cell (HC) transfected with (III); (7) antibody (IV) which selectively binds (I); (8) production of (I); (9) detecting (M1) the presence of (II) in a sample by contacting the sample with a nucleic acid probe or primer which selectively hybridizes to (II), and determining whether the probe or primer binds to (II) in the sample; (10) kit (V) comprising a compound which selectively binds to (I) or hybridizes to (II), and instructions for use; and (11) modulating (M2) the activity of (I) by contacting (I) or a cell expressing (I) with a compound which binds to (I).

WIDER DISCLOSURE - Also disclosed are: (1) isolated NA antisense to (II); (2) diagnostic assay for identifying the presence or absence of a genetic alteration characterized by at least one of aberrant modification or mutation of a gene encoding a **CARK** protein, mis-regulation of the gene, and aberrant post-translational modification of a **CARK** protein; (3) nucleic acid molecule that differs from S2, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-1530; (4) a non-**human** ortholog of (I); (5) nucleic acid molecule encoding (I) that contains changes in (aa) residues that are not essential for activity; (6) **CARK** chimeric or fusion proteins; and (7) agent which modulates expression or activity of (I).

BIOTECHNOLOGY - Preparation: (I) is produced by culturing HC in an appropriate culture medium to produce (I) (claimed). Preferred Polypeptide: (I) further comprises heterologous (aa) sequences. Preferred Vector: (III) is an expression vector. Preferred Method: In M1, the sample comprises mRNA molecules and is contacted with a nucleic acid probe.

ACTIVITY - Cardiant; Hypotensive; Cytostatic. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - (IV) is useful for detecting the presence of (I) in a sample by contacting the sample with (IV), and determining whether (IV) binds to (I) in the sample. (I) is useful for identifying a compound which binds to (I) by contacting (I), or a cell expressing (I) with a test compound, and determining whether (I) binds to the test compound. (I) is useful for identifying a compound which modulates the activity of (I) by contacting (I) with a test compound and determining the effect of the test compound on the activity of (I) (claimed). (I) or (II) is useful as modulating agents for regulating a variety of cellular processes, e.g., cardiac cellular process, for modulating the phosphorylation state of a **CARK** molecule or one or more proteins involved in cellular growth or differentiation, for modulating cell behavior or as targets and therapeutic agents controlling cardiac cell proliferation,

differentiation, hypertrophy and migration, for modulating intra-or inter-cellular signaling and/or gene transcription, for modulating cell proliferation, growth, differentiation, survival and/or migration, for regulating transmission of signals from cellular receptors, for modulating entry of cells, e.g., cardiac precursor cells, into mitosis, or for regulating cytoskeletal function. (I) or (II) is useful for treating cellular growth related disorders which include cardiovascular disorders (such as heart failure, hypertension), and proliferative and/or differentiative disorders (such as cancer). (I), (II) or (IV) is useful in screening assays, detection assays (e.g., chromosomal mapping, tissue typing, forensic biology), predictive medicine (e.g., diagnostic assays, prognostic assays, monitoring clinical trials and pharmacogenomics), and in methods of treatment (e.g., therapeutic and prophylactic). (I) is useful as an immunogen to generate antibodies that bind (I). (I) is useful to screen for naturally occurring **CARK** substrates, and to screen for drugs or compounds which modulate **CARK** activity. (I) is useful as a bait protein in a yeast two-hybrid or three-hybrid assay and to identify other proteins which bind to or interact with **CARK** and or involved in the **CARK** activity. (II) is useful as hybridization probe to identify (II), or as polymerase chain reaction (PCR) primer for the amplification or mutation of (II). (II) is useful in gene therapy, to express (I), to detect **CARK** mRNA or a genetic alteration in a **CARK** gene, and to modulate **CARK** activity. (II) is useful to map their respective genes on a chromosome, e.g. to locate gene regions associated with genetic disease or to associate **CARK** with the disease, to identify an individual from a minute biological sample (tissue typing), and to aid in forensic identification of the biological sample. (I) or (II) is useful as a query sequence to perform a search against public databases to, for example, identify other family members or related sequences. HC is useful for producing non-**human** transgenic animals. (IV) is useful to isolate and purify (I), to detect (I) and to diagnostically monitor protein levels in tissue as part of a clinical testing procedure.

ADMINISTRATION - A pharmaceutical composition comprising (I), (II) or (V) is administered by parenteral, e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (topical), transmucosal, or rectal route at a dose of 0.001-30 mg/kg, preferably 1-10 mg/kg, more preferably 5-6 mg/kg.

EXAMPLE - Identification and characterization of the genes encoding **human cardiac-related ankyrin-repeat** protein kinase (**CARK**) and rat **CARK** was as follows: The **human CARK** gene was isolated from cDNA library which was prepared from tissue obtained from subjects suffering from congestive heart failure of ischemic and idiopathic origin. Briefly, a cardiac tissue sample was obtained from a biopsy of four patients suffering from congestive heart failure. mRNA was isolated from the cardiac tissue and a cDNA library was prepared. Positive clones were isolated from these libraries using appropriate primers. The sequence of the positive clone was determined and found to contain an open reading frame. The nucleotide sequence encoding the **human CARK** protein comprised about 3025 nucleic acids. The protein encoded by this nucleic acid comprised abut 835 (aa)s. A clone containing the rat **CARK** cDNA was also identified. The nucleotide sequence encoding the rat **CARK** protein comprised about 3026 nucleic acids. The protein encoded by this nucleic acid comprised about 835 (aa)s. (158 pages)

L9 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:696560 HCAPLUS
DOCUMENT NUMBER: 137:227755
TITLE: Protein and cDNA sequences of novel **human** and rat **CARK** (**cardiac-related ankyrin repeat** protein kinase) and uses thereof

INVENTOR(S): Raju, Jeyaseelan
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 94 pp., Cont.-in-part of U.S. Ser. No. 458,457.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002127684	A1	20020912	US 2001-947199	20010905
US 6660490	B2	20031209		
US 6261818	B1	20010717	US 1999-291839	19990414
US 6500654	B1	20021231	US 1999-458457	19991210
WO 2003020912	A2	20030313	WO 2002-US28300	20020904
WO 2003020912	A3	20030828		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1430070	A2	20040623	EP 2002-757606	20020904
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004110232	A1	20040610	US 2003-626173	20030724
PRIORITY APPLN. INFO.:			US 1998-111938P	P 19981211
			US 1999-291839	A2 19990414
			US 1999-458457	A2 19991210
			US 2001-947199	A 20010905
			WO 2002-US28300	W 20020904

AB The invention provides **human** and rat protein and cDNA sequences encoding **CARK** (**cardiac-related ankyrin repeat** protein kinase). The invention also provides antisense nucleic acid mols., recombinant expression vectors containing **CARK** nucleic acid mols., host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which a **CARK** gene has been introduced or disrupted. The invention still further provides isolated **CARK** proteins, fusion proteins, antigenic peptides and anti-**CARK** antibodies. Diagnostic methods utilizing compns. of the invention are also provided.

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E2           3      RAJU IVATURY S/AU
E3         109 --> RAJU J/AU
E4           1      RAJU J A S/AU
E5           1      RAJU J AYYAPA/AU
E6           5      RAJU J AYYAPPA/AU
E7           1      RAJU J B/AU
E8           3      RAJU J D/AU
E9           8      RAJU J M/AU
E10          3      RAJU J N/AU
E11         81      RAJU J R/AU
E12         11      RAJU J S/AU
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L10         109 "RAJU J"/AU

=> d his

     (FILE 'HOME' ENTERED AT 09:54:24 ON 14 SEP 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 09:54:57 ON 14 SEP 2004
L1           14 S "CARK"
L2            4 S "CARDIAC-RELATED ANKYRIN-REPEAT"
L3           14 S L1 OR L2
L4      3904375 S MODULATOR? OR INHIBITOR? OR ACTIVATOR?
L5      8679450 S IDENTIF? OR FIND? OR SCREEN?
L6       638317 S L4 AND L5
L7            0 S L3 AND L6
L8           13 DUP REM L3 (1 DUPLICATE REMOVED)
L9            2 S HUMAN AND L8
              E RAJU J/AU
L10         109 S E3

=> s l3 and l10
L11           2 L3 AND L10

=> d 1-2 ibib ab

L11   ANSWER 1 OF 2  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-13047  BIOTECHDS
TITLE:            Novel isolated cardiac-related
                  ankyrin-repeat protein kinase polypeptide,
                  useful for treating cellular growth related disorders which
                  include cardiovascular disorders and proliferative and/or
                  differentiative disorders;
                     vector-mediated gene transfer and expression in host cell
                     for recombinant protein production for use in disease
                     diagnosis, gene therapy and pharmacogenomics
AUTHOR:           RAJU J
PATENT ASSIGNEE:  MILLENNIUM PHARM INC
PATENT INFO:      WO 2003020912 13 Mar 2003
APPLICATION INFO: WO 2002-US28300 4 Sep 2002
PRIORITY INFO:    US 2001-947199 5 Sep 2001; US 2001-947199 5 Sep 2001
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2003-290188 [28]
AB    DERWENT ABSTRACT:
      NOVELTY - An isolated cardiac-related ankyrin
      -repeat protein kinase (CARK) polypeptide (I),
      comprising an allelic variant of a polypeptide having a sequence (S1) of
      835 amino acids (aa), encoded by a nucleic acid molecule (NA) that
      hybridizes to a sequence (S2) of 3025, 2505 or 3026 base pairs, or a
      polypeptide encoded by a NA 60% homologous to S2, or fragment of S1,
      where S1 and S2 are given in specification, is new.
           DETAILED DESCRIPTION - (I) is selected from a naturally occurring
      allelic variant of S1 encoded by a NA which hybridizes to NA comprising
      S2 under stringent conditions, a polypeptide encoded by a NA comprising a
      sequence which is at least 60% homologous to S2, a fragment comprising at
      least 15 contiguous (aa)s of S1, and a polypeptide comprising an (aa)
      sequence which is at least 60% homologous to S1. INDEPENDENT CLAIMS are
      also included for the following: (1) isolated NA (II) selected from a NA
      comprising a sequence of S2, a NA which encodes a polypeptide comprising
      S1, a NA comprising the sequence contained in the plasmid deposited with
      ATCC as Accession Number PTA-1530, a NA which encodes the naturally
      occurring allelic variant of S1, a NA comprising a sequence which is at
      least 60% homologous to S2 or its complement, a NA comprising a fragment
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of at least 467 nucleotides of S2 or its complement, a NA which encodes a polypeptide comprising a sequence at least about 60% homologous to S1, and a NA which encodes a fragment of S1, where the fragment comprises at least 15 contiguous (aa)s of S1; (2) an isolated NA which hybridizes to (II) under stringent conditions; (3) isolated NA comprising a sequence which is complementary to the sequence of (II); (4) isolated NA comprising (II), and a nucleotide sequence encoding a heterologous polypeptide; (5) vector (III) comprising (II); (6) host cell (HC) transfected with (III); (7) antibody (IV) which selectively binds (I); (8) production of (I); (9) detecting (M1) the presence of (II) in a sample by contacting the sample with a nucleic acid probe or primer which selectively hybridizes to (II), and determining whether the probe or primer binds to (II) in the sample; (10) kit (V) comprising a compound which selectively binds to (I) or hybridizes to (II), and instructions for use; and (11) modulating (M2) the activity of (I) by contacting (I) or a cell expressing (I) with a compound which binds to (I).

WIDER DISCLOSURE - Also disclosed are: (1) isolated NA antisense to (II); (2) diagnostic assay for identifying the presence or absence of a genetic alteration characterized by at least one of aberrant modification or mutation of a gene encoding a **CARK** protein, mis-regulation of the gene, and aberrant post-translational modification of a **CARK** protein; (3) nucleic acid molecule that differs from S2, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number PTA-1530; (4) a non-human ortholog of (I); (5) nucleic acid molecule encoding (I) that contains changes in (aa) residues that are not essential for activity; (6) **CARK** chimeric or fusion proteins; and (7) agent which modulates expression or activity of (I).

BIOTECHNOLOGY - Preparation: (I) is produced by culturing HC in an appropriate culture medium to produce (I) (claimed). Preferred Polypeptide: (I) further comprises heterologous (aa) sequences. Preferred Vector: (III) is an expression vector. Preferred Method: In M1, the sample comprises mRNA molecules and is contacted with a nucleic acid probe.

ACTIVITY - Cardiant; Hypotensive; Cytostatic. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - (IV) is useful for detecting the presence of (I) in a sample by contacting the sample with (IV), and determining whether (IV) binds to (I) in the sample. (I) is useful for identifying a compound which binds to (I) by contacting (I), or a cell expressing (I) with a test compound, and determining whether (I) binds to the test compound. (I) is useful for identifying a compound which modulates the activity of (I) by contacting (I) with a test compound and determining the effect of the test compound on the activity of (I) (claimed). (I) or (II) is useful as modulating agents for regulating a variety of cellular processes, e.g., cardiac cellular process, for modulating the phosphorylation state of a **CARK** molecule or one or more proteins involved in cellular growth or differentiation, for modulating cell behavior or as targets and therapeutic agents controlling cardiac cell proliferation, differentiation, hypertrophy and migration, for modulating intra-or inter-cellular signaling and/or gene transcription, for modulating cell proliferation, growth, differentiation, survival and/or migration, for regulating transmission of signals from cellular receptors, for modulating entry of cells, e.g., cardiac precursor cells, into mitosis, or for regulating cytoskeletal function. (I) or (II) is useful for treating cellular growth related disorders which include cardiovascular disorders (such as heart failure, hypertension), and proliferative and/or differentiative disorders (such as cancer). (I), (II) or (IV) is useful in screening assays, detection assays (e.g., chromosomal mapping, tissue typing, forensic biology), predictive medicine (e.g., diagnostic assays, prognostic assays, monitoring clinical trials and pharmacogenomics), and in methods of treatment (e.g., therapeutic and prophylactic). (I) is useful as an immunogen to generate antibodies that bind (I). (I) is

useful to screen for naturally occurring **CARK** substrates, and to screen for drugs or compounds which modulate **CARK** activity. (I) is useful as a bait protein in a yeast two-hybrid or three-hybrid assay and to identify other proteins which bind to or interact with **CARK** and or involved in the **CARK** activity. (II) is useful as hybridization probe to identify (II), or as polymerase chain reaction (PCR) primer for the amplification or mutation of (II). (II) is useful in gene therapy, to express (I), to detect **CARK** mRNA or a genetic alteration in a **CARK** gene, and to modulate **CARK** activity. (II) is useful to map their respective genes on a chromosome, e.g. to locate gene regions associated with genetic disease or to associate **CARK** with the disease, to identify an individual from a minute biological sample (tissue typing), and to aid in forensic identification of the biological sample. (I) or (II) is useful as a query sequence to perform a search against public databases to, for example, identify other family members or related sequences. HC is useful for producing non-human transgenic animals. (IV) is useful to isolate and purify (I), to detect (I) and to diagnostically monitor protein levels in tissue as part of a clinical testing procedure.

ADMINISTRATION - A pharmaceutical composition comprising (I), (II) or (V) is administered by parenteral, e.g., intravenous, intradermal, subcutaneous, oral (e.g., inhalation), transdermal (topical), transmucosal, or rectal route at a dose of 0.001-30 mg/kg, preferably 1-10 mg/kg, more preferably 5-6 mg/kg.

EXAMPLE - Identification and characterization of the genes encoding human **cardiac-related ankyrin-repeat** protein kinase (**CARK**) and rat **CARK** was as follows: The human **CARK** gene was isolated from cDNA library which was prepared from tissue obtained from subjects suffering from congestive heart failure of ischemic and idiopathic origin. Briefly, a cardiac tissue sample was obtained from a biopsy of four patients suffering from congestive heart failure. mRNA was isolated from the cardiac tissue and a cDNA library was prepared. Positive clones were isolated from these libraries using appropriate primers. The sequence of the positive clone was determined and found to contain an open reading frame. The nucleotide sequence encoding the human **CARK** protein comprised about 3025 nucleic acids. The protein encoded by this nucleic acid comprised abut 835 (aa)s. A clone containing the rat **CARK** cDNA was also identified. The nucleotide sequence encoding the rat **CARK** protein comprised about 3026 nucleic acids. The protein encoded by this nucleic acid comprised about 835 (aa)s. (158 pages)

L11 ANSWER 2 OF 2 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2000-11607 BIOTECHDS
TITLE: New polynucleotide encoding **cardiac-related ankyrin-repeat** protein-kinase, useful for treating disorders such as cardiovascular disorders, e.g. heart failure and cell differentiation disorders, e.g. cancer ;
vector-mediated gene transfer and expression in host cell, antibody, DNA probe and DNA primer
AUTHOR: **Raju J**
PATENT ASSIGNEE: Millennium-Pharm.
LOCATION: Cambridge, MA, USA.
PATENT INFO: WO 2000034330 15 Jun 2000
APPLICATION INFO: WO 1999-US29465 10 Dec 1999
PRIORITY INFO: US 1999-291839 14 Apr 1999; US 1998-111938 11 Dec 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2000-431275 [37]
AB A polynucleotide encoding a **cardiac-related ankyrin-repeat** protein-kinase (EC-2.7.1.37) (**CARK**) containing a sequence of 3,025, 2,505, 3,026 or 2,505 bp as defined in the specification, is new. Also claimed are: a nucleic

encoding a protein of 835 amino acids; an expression vector; a host cell; a method of producing the protein; an antibody; a method for detecting the presence of the protein; a method for detecting the presence of the polynucleotide using a DNA probe or DNA primer; a kit containing a compound that specifically binds to the protein or polynucleotide; a method for identifying a compound that specifically binds to the protein; a method for modulating the activity of the protein; and a method for identifying a compound which modulates that activity of the protein. The polynucleotides is useful for detecting nucleic acid molecule especially mRNA in a sample, **CARK** encoded by the polynucleotide is useful for treating disorders associated with upregulation or downregulation of cellular proliferation such as disorders concerned with cardiovascular disorders and disorders associated with differentiation of cells such as cancer and sarcoma. (161pp)

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FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:54:57 ON 14 SEP 2004

L1	14	S	"CARK"
L2	4	S	"CARDIAC-RELATED ANKYRIN-REPEAT"
L3	14	S	L1 OR L2
L4	3904375	S	MODULATOR? OR INHIBITOR? OR ACTIVATOR?
L5	8679450	S	IDENTIF? OR FIND? OR SCREEN?
L6	638317	S	L4 AND L5
L7	0	S	L3 AND L6
L8	13		DUP REM L3 (1 DUPLICATE REMOVED)
L9	2	S	HUMAN AND L8
		E	RAJU J/AU
L10	109	S	E3
L11	2	S	L3 AND L10

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5	L5	1	l1 and l4
6	L6	53012	hybridiz$3
7	L7	1	l1 and l6
8	L8	83	"0.2XSSC"
9	L9	0	l1 and l8
10	L10	770727	"65"
11	L11	1	l1 and l10
12	L12	1	6500654.pn.
13	L13	0	l8 and l12

	L #	Hits	Search Text
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16	L16	5	"cardiac-related" adj "ankyrin-repeat"
17	L17	27	"CARK"
18	L18	1303708	modulat$3 or activat$3 or inhibit$3
19	L19	11	l17 and l18
20	L20	861	RAJU
21	L21	5	l17 and l20

	Issue Date	Pages	Document ID	Title
1	20040610	95	US 20040110232 A1	Novel cark protein and nucleic acid molecules and uses therefor
2	20020912	94	US 20020127684 A1	Novel cark protein and nucleic acid molecules and uses therefor
3	20031209	91	US 6660490 B2	CARK protein and nucleic acid molecules and uses therefor
4	20021231	86	US 6500654 B1	CARK protein and nucleic acid molecules and uses therefor
5	20010717	61	US 6261818 B1	CARK protein and nucleic acid molecules and uses therefor

	Issue Date	Pages	Document ID	Title
1	20040610	95	US 20040110232 A1	Novel cark protein and nucleic acid molecules and uses therefor
2	20021226	51	US 20020197568 A1	Biochemical analysis unit and method of producing thereof
3	20020912	94	US 20020127684 A1	Novel cark protein and nucleic acid molecules and uses therefor
4	20040217	15	US 6693236 B1	User interface for simultaneous management of owned and unowned inventory
5	20031209	91	US 6660490 B2	CARK protein and nucleic acid molecules and uses therefor
6	20021231	86	US 6500654 B1	CARK protein and nucleic acid molecules and uses therefor
7	20020402	14	US 6366957 B1	Computer system having remote wake-up function and remote wake-up method thereof
8	20010717	61	US 6261818 B1	CARK protein and nucleic acid molecules and uses therefor
9	19980714	14	US 5780470 A	Melatonergic indanyl piperazines

	Issue Date	Pages	Document ID	Title
10	19970211	20	US 5602993 A	Method and system for revising data in a distributed data communication system
11	19721107	152	US 3702381 A	TELEPHONE SWITCHING SYSTEM INCLUDING TOLL SERVICE DESK

	Issue Date	Pages	Document ID	Title
1	20040610	95	US 20040110232 A1	Novel cark protein and nucleic acid molecules and uses therefor
2	20020912	94	US 20020127684 A1	Novel cark protein and nucleic acid molecules and uses therefor
3	20031209	91	US 6660490 B2	CARK protein and nucleic acid molecules and uses therefor
4	20021231	86	US 6500654 B1	CARK protein and nucleic acid molecules and uses therefor
5	20010717	61	US 6261818 B1	CARK protein and nucleic acid molecules and uses therefor